THE COMMONWEALTH OF MASSACHUSETTS
EXECUTIVE OFFICE OF ENERGY AND ENVIRONMENTAL AFFAIRS

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MDAR
MASSACHUSETTS DEPARTMENT OF AGRICULTURAL RESOURCES

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GOVERNOR	LIEUTENANT GOVERNOR	SECRETARY	COMMISSIONER

PESTICIDE BOARD SUBCOMMITTEE MEETING MINUTES

September 17, 2024

BOARD MEMBERS IN ATTTENDANCE

Michael Moore, DPH, Food Protection Program, (Chair)	Present
Taryn LaScola, MDAR, Designee for Commissioner Randle	Present
Meg Blanchet, DPH, Designee for Commissioner Goldstein	Present
Nicole Keleher, DCR, Designee for Commissioner Arrigo	Present
Richard Berman, Commercial Applicator	Present

The Board did meet or exceed the minimum number (3) of members present to form a quorum and conduct business.

A. REVIEW OF MINUTES FOR August 20, 2024

Motion: R. Berman
Second: N. Keleher
Discussion: None
In Favor: R. Berman, N. Keleher, M. Moore
Opposed: None
Abstained: 2

B. PRODUCT REGISTRATIONS

Motion That the Pesticide Board Subcommittee registers the pesticide products listed on the EIPAS PR September 17, 2024, Subcommittee cover sheet with the exception of the following products:

1. Temprid Ready-to-Spray Insecticide, EPA Reg. No. 101563-151,
2. Premise Pro Insecticide, EPA Reg. No. 101563-115,
3. Smokeshow, EPA Reg. No. 83529-112-53883,
4. Topsite 2.5G Herbicide, EPA Reg. No. 103184-7,
5. Sprakil SK-13 Granular Weed Killer, EPA Reg. No. 103184-3,
6. Nutrite Professional Turf Fertilizer with Merit 0.2 Plus 0-0-7, EPA Reg. No. 101563-76-93243,
7. Nutrite Professional Turf Fertilizer with 0.225% ALLECTUS Insecticide 0-0-7, EPA Reg. No. 101563-105-93243,
8. Masterline I MaxxPro Insecticide in Water Soluble Packets, EPA Reg. No. 101563-67-73748, and
9. Calantha, EPA Reg. No. 94614-2.

Moved: R. Berman
Second: T. LaScola
Discussion: None
In Favor: M. Blanchet, R. Berman, T. LaScola, N. Keleher, M. Moore
Opposed: None
Abstained: None

Motion: That the Pesticide Board Subcommittee has determined that the use of the following products may pose unreasonable adverse effects to the environment as well as to pollinators, when taking into account the economic, social, and environmental costs and benefits of their use in the Commonwealth and are thereby restricted. This is pursuant to the Subcommittee's decision on March 1, 2021, to modify the registration classification of products containing neonicotinoids, including **imidacloprid**, that have outdoor non-structural uses or outdoor non-agricultural uses on the label from general to state restricted use:

1. Temprid Ready-to-Spray Insecticide, EPA Reg. No. 101563-151,
2. Premise Pro Insecticide, EPA Reg. No. 101563-115,
3. Nutrite Professional Turf Fertilizer with Merit 0.2 Plus 0-0-7, EPA Reg. No. 101563-76-93243,
4. Nutrite Professional Turf Fertilizer with 0.225% ALLECTUS Insecticide 0-0-7, EPA Reg. No. 101563-105-93243,
5. Masterline I MaxxPro Insecticide in Water Soluble Packets, EPA Reg. No. 101563-67-73748, all containing imidacloprid

Moved: R. Berman
Second: T. LaScola
Discussion: None
In Favor: M. Blanchet, R. Berman, T. LaScola, N. Keleher, M. Moore
Opposed: None
Abstained: None

Motion: That the Pesticide Board Subcommittee has determined that the use of the following products

1. Smokeshow, EPA Reg. No. 83529-112-53883, containing metribuzin and sulfentrazone,
2. Topsite 2.5G Herbicide, EPA Reg. No. 103184-7, containing diuron, and
3. Sprakil SK-13 Granular Weed Killer, EPA Reg. No. 103184-3, containing diuron

may cause an unreasonable risk to man or the environment, when taking into account the economic, social, and environmental costs and benefits of their use. This determination is based upon the leaching potential and toxicological concern of these substance as defined in the "Protection of Groundwater Supplies from Non-Point Source Pesticide Contamination" Regulations. Therefore, the Subcommittee hereby modifies the registration classification of agricultural/commercial pesticide products containing **sulfentrazone, metribuzin, and diuron** from general to restricted use for groundwater concerns.

Moved: R. Berman
Second: T. LaScola
Discussion: None
In Favor: M. Blanchet, R. Berman, T. LaScola, N. Keleher, M. Moore
Opposed: None
Abstained: None

D. NEW ACTIVE INGREDIENT MOTION

Miller presented information on the new active ingredient ledprona, formulated in the product Calantha (EPA Reg. No. 94614-2), a selective bioinsecticide targeting the Colorado Potato Beetle. Ledprona is 0.8% of the formulation by weight, with the rest over 75% water and ~21% other co-formulants. The liquid product is diluted and then applied as a foliar spray.

The ledprona mode of action is Group 35, 'RNA interference-mediated target suppressor', and is the only active ingredient (AI) in this group to date. In 2015, EPA registered the first double strand RNA-based insecticidal product, which was a plant incorporate protectant (PIP) called DvSnf7, in corn for control of Western Corn Rootworm.

Ledprona is a sprayable double-stranded RNA molecule designed to target the messenger RNA (mRNA) sequence of the potato beetle proteosome subunit beta type-5 (PSMB5). This RNA interference, which is a natural process in cells, is a mechanism that many eukaryotes use to regulate gene expression. It can also serve as a defense against transposable elements and RNA-based viruses by targeting them for degradation. Ingestion of ledprona by potato beetle larvae or adults (not eggs) leads to the downregulation of PSMB5 protein, a critical protein for clearing waste from cells, and ultimately leads to death of the potato beetle.

This AI was first approved for an Experimental Use Permit (EUP) in 2023, where the EUP test sites were in 10 states, including Idaho, Maine, and New York. The Section 3 registration is initially for 2 years, which is standard.

The signal word on the Calantha label is 'Caution', with text immediately underneath stating, "Prolonged or frequently repeated skin contact may cause allergic reactions in some individuals." Baseline PPE is required (long-sleeved shirt, long pants, shoes, socks) as well as protective eyewear. Applicators and handlers are directed to wear a NIOSH-approved particulate filtering facepiece or elastomeric particulate respirator with any N*, R, or P filter. Alternatively, one can wear a NIOSH-approved powered air purifying respirator with an HE filter.

The restricted entry interval (REI) is 4 hours after treatment, though early entry involving contact with treated materials is permitted if PPE is worn.

Calantha is only labeled for controlling Colorado Potato Beetle on potato plants. The spray solution coats plant foliage and can be ingested by the beetle at any post-hatching stage in its life cycle, though maximum efficacy occurs with young larvae. Feeding typically stops within 3 days of application, but mortality may take 7 to 10 days. The application rate is 0.134 oz AI/acre, or ~16 fl. oz of product. No more than 4 applications per year are permitted and resistance management limits areas with only one generation of beetle per growing season to only 2 applications per year. There is no preharvest interval.

The product is considered compatible with tank mixing, which was not part of the EUP and is a change for the Section 3 registration. It can be applied with ground sprayers, fixed- or rotary-winged aircraft, or via sprinkler-type chemigation. The label includes both spray drift advisory language (in the form of qualitative nozzle shield and droplet size recommendations) as well as required restrictions. Both ground and aerial applications have specific wind speed and boom height limits. Aerial applications are prohibited during temperature inversions. Chemigation restrictions require that application only be through overhead

sprinkler-type systems with uniform coverage of the crop canopy and water amounts equivalent to less than 0.2" of irrigation. Label instructions specify chemigation equipment and system requirements to prevent water contamination.

Studies indicate Calantha has a low risk profile for human health. Mammalian toxicity data (for both the technical AI ledprona and the Calantha formulation) for acute oral toxicity, acute dermal toxicity, acute inhalation toxicity, primary irritation, and primary dermal irritation supported classification as Toxicity Category IV, for low to negligible toxicity. Studies did not find ledprona technical to be a dermal sensitizer. However, Calantha tested separately was considered a weak sensitizer.

Because this is a novel mode of action that involves gene silencing, EPA utilized bioinformatic analysis to try to predict the likelihood of off-target effects of the ledprona double strand RNA sequence aligned to the human transcriptome. Two potential "off-target" transcripts in the human genome for three ledprona 21-nucleotide length sequences were identified, but from further analysis EPA concluded they were unlikely to affect these genes *in vivo*. This was specifically considered in the case of inhalation risk to lung cells. However, the highest potential exposure is several orders of magnitude lower than levels shown to be effective in animal studies that tested the efficacy of small interfering RNA as inhalable therapeutics. EPA states, "While it cannot be excluded that one of the two putative human transcripts that show homology to Ledprona may be expressed in the lung, based on the demonstrated specificity of Ledprona to CPB and closely related species and considerations regarding the long double strand RNA processing in the cell, that hazard is considered negligible."

Digestibility studies examined how quickly ledprona and Calantha are degraded in simulated gastric and intestinal fluids. Both degraded within 20 and 10 minutes, respectively. Additionally, the applicant submitted a study evaluating the permeability, or uptake, of the technical AI in human epithelial colorectal adenocarcinoma cells as a model of the intestinal epithelial barrier. The uptake rate range of ledprona was ~3-20 times slower than the low-absorption control, suggesting low uptake is expected.

To satisfy requirements for a 90-day Oral Toxicity study, the Prenatal Developmental Toxicity study, Bacterial Reverse Mutation test, and In vitro Mammalian Cell Gene Mutation test, the applicant submitted rationales to waive the submission of these studies. These rationales were based on the available acute toxicity studies indicating very low toxicity, the low exposure label use pattern, environmental fate data indicating rapid degradation, and formulation-specific digestibility studies demonstrating rapid degradation in mammalian stomach and intestines.

Quantitative dietary and drinking water exposure and risk assessments for humans were not conducted because dietary exposure to residue in food is expected to be negligible. A residential exposure assessment was not conducted or required because ledprona is not proposed for residential use. Bystander exposure may occur post-application, such as contact with treated foliage or through spray drift, but adherence to label language is expected to make such exposure negligible. Low occupational exposure is anticipated due to the low toxicological profile of the AI. EPA has concluded there is reasonable certainty that no harm will result to the US population, including infants and children, from aggregate exposure to ledprona residues.

Environmental risks are also considered low. Aerobic degradation was measured in a variety of agricultural soils, with DT50 values ranging from 0.5 to 2.9 days. For all soils tested, the DT90 was within 4 days, though soils still maintained a low but detectable concentration by the end of the study at Day 12. Studies of the aerial 0.2 grams/liter application rate observed microbial degradation of ledprona technical and Calantha within 25 and 80 hours, respectively.

Potential aquatic environment exposure would likely be due to washout and run-off. However, unformulated double-strand RNA generally degrades quickly once in aquatic systems due to microbial activity and

hydrolysis. The submitted aerobic aquatic degradation study for Calantha calculated DT50 values of 1.3 and 1.9 days for two representative aquatic environments.

Above ground terrestrial nontarget organisms are most likely to be exposed, though soil-dwelling organisms may have indirect contact with the product. Risk to nontarget organisms is considered low due to the low label rates of ledprona and restrictions on the label to minimize drift.

EPA has determined that exposure to Calantha by nontarget organisms is not expected to pose a hazard to any non-coleopteran. Bioinformatic analyses demonstrated a lack of similarity between ledprona and genomes/transcriptomes of a range of nontarget organisms. This was further supported by toxicity studies indicating no effects upon any taxa tested (with the exception of two closely related beetles), the low application rates and rapid degradation times within soil, aquatic sediment, and larval CPB gut fluids from microbial activity, and known physiological barriers to double strand RNA present within vertebrate species.

This AI has been assessed for compliance with the Endangered Species Act. The combination of scientific rationales, bioinformatics analyses, and bioassay results indicate the specificity of ledprona to beetles (Coleoptera). While no effects were observed in the coleopteran Ladybird Beetle, effects in two beetles closely related to CPB, the Red Flour Beetle and the Southern Corn Rootworm, were identified. Therefore, detailed exposure risk analyses were conducted for the four coleopteran listed species - all beetles - where there is potential for exposure due to known ranges and potato crop locations. Of these, three have habitat in Massachusetts: the American Burying Beetle on Nantucket, the Northeastern beach tiger beetle along several south shores of New England, and the Puritan tiger beetle along the Connecticut River. Only the Puritan Tiger Beetle has known overlap between potato crops and habitat. Based on those analyses, EPA has made a 'No Effect' determination under the Endangered Species Act for all listed species.

Ledprona does not meet the criteria for being classified as a potential groundwater contaminant in Massachusetts.

Move: that the Pesticide Board Subcommittee approve the product registration for Calantha, EPA Reg. No. 94614-2, containing the new active ingredient ledprona, which has never before been registered in Massachusetts.

E. NEW BUSINESS

There was no new business brought forward.

F. ADJOURN

Motion: To adjourn the September 17, 2024, Subcommittee Meeting.

Moved: T. LaScola
Second: R. Berman
Discussion: None
In Favor: M. Blanchet, R. Berman, T. LaScola, N. Keleher, M. Moore
Opposed: None
Abstained: None